

## Abstracts

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### D-dimer and Factor VIII are Independent Risk Factors for Recurrence After Anticoagulation Withdrawal for a First Idiopathic Deep Venous Thrombosis

Cosmi B, Legnani C, Cini M. *Thromb Res* 2008;122:610-7.

**Conclusion:** Elevated levels of D-dimer and factor VIII at 30  $\pm$  10 days after cessation of vitamin K antagonist (VKA) therapy for a first episode of idiopathic proximal deep venous thrombosis (DVT) are independent risk factors for recurrent venous thromboembolism (VTE).

**Summary:** The optimal duration of VKA therapy after a first episode of VTE is unknown. It appears VKA extension after unprovoked VTE can reduce the risk of recurrent VTE but at the potential price of increased bleeding. There is therefore intense interest in stratifying patients with idiopathic VTE with respect to risk factors that may increase rates of recurrence. The specific objective of this study was to assess the risk of recurrence of VTE associated with elevated D-dimer levels and factor VIII levels after withdrawal of VKA therapy for symptomatic idiopathic proximal VTE.

Consecutive outpatients with the first episode of idiopathic proximal DVT were enrolled into the study after cessation of VKA therapy. At 30  $\pm$  10 days after cessation of VKA therapy, levels of D-dimer (cutoff value, 500 ng/mL) and chromogenic factor VIII, as well as inherited thrombophilias were determined. Follow-up extended for 2 years.

Overall recurrence rate of VTE was 16.4% (55 of 336; 95% confidence interval [CI], 13%-21%). The multivariate hazard ratio for recurrence was 2.45 (95% CI, 1.24-4.99) for abnormal D-dimer and 2.76 (95% CI, 1.57-4.85) for factor VIII >75th percentile (2.42  $\mu$ g/mL). The values were adjusted for age, sex, and thrombophilia. Compared with normal levels of D-dimer and factor VIII, the multivariate hazard ratio was 4.5 (95% CI, 1.7-12.2) for normal D-dimer levels with factor VIII >2.42 U/mL, and 2.7 (95% CI, 1.2-6.6) and 7.1 (95% CI, 2.8-17.6) for abnormal D-dimer with factor VIII, respectively, below and above 2.42 U/mL.

**Comment:** The appropriate length of treatment with VKA therapy for patients with idiopathic VTE is unknown. The data suggest the longer the treatment period with VKA, the less the recurrence rates of VTE. Of course, VKAs are associated with increased risk of bleeding and are inconvenient for the patient. There is therefore intense interest in stratifying risk among those patients with idiopathic VTE. This is another study that attempts to do just that. The percentage of patients with both normal D-dimer and factor VIII <75th percentile was 37%. This implies that at least a third of patients with idiopathic VTE have a low risk of VTE recurrence. Larger studies are warranted to determine if the combination of factor VIII and D-dimer analysis can be used to tailor duration of VKA therapy after idiopathic VTE.

### Drug-Eluting or Bare-Metal Stents for Acute Myocardial Infarction

Mauri L, Silbaugh TS, Garg P. *N Engl J Med* 2008;359:1330-42.

**Conclusion:** Treatment with drug-eluting stents in patients with acute myocardial infarction (AMI) results in a decreased 2-year mortality rate and a reduction in need for repeat revascularization procedures compared with treatment of AMI with bare-metal stents.

**Summary:** The Massachusetts Department of Public Health in 2002 established a requirement that hospitals in that state providing interventional cardiology services collect data on percutaneous coronary interventions (PCIs). Data are collected by trained data collectors and are submitted electronically to the Massachusetts Data Analysis Center. Analysis of this data forms the basis of this study. The authors identify patients undergoing PCI using coronary stents with an indication of AMI. Data were analyzed from April 1, 2003, to September 30, 2004. The authors used a propensity-score matching analysis on three patient groups: all patients with AMI, all patients with AMI and ST-segment elevation, and all patients with AMI without ST-segment elevation. Analysis was based on clinical, procedural, hospital, and insurance information collected at the time of the PCI procedure. Vital statistics records were used to determine risk of death in patients receiving drug-eluting stents and those receiving bare-metal stents.

During the study, 7217 patients were treated for AMI, of which 4016 were treated with drug-eluting stents and 3201 with bare-metal stents. Matched pair analysis showed the 2-year risk-adjusted mortality rates were lower for drug-eluting stents among all patients with AMI (10.7% vs 12.8%,  $P = .02$ ). The 2-year risk-adjusted mortality rate was also lower among patients with AMI with ST-segment elevation (8.5% vs 11.6%,  $P = .008$ ) and among patients with AMI without ST-segment elevation (12.8% vs 15.6%,  $P = .04$ ). Repeat revascularization rates in all groups were also significantly reduced with drug-eluting stents.

**Comment:** During the time of this study, patients with MI accounted for 40% of coronary stent procedures in Massachusetts. Drug-eluting stents appeared to reduce restenosis in the coronary circulation after stent treatment. Previous studies have reported an association between restenosis and risk of death for MI; therefore, the findings of the study make inherent sense. These data were observational, however, and although the authors tried to make their groups comparable, there are potential confounding variables. In particular, during the time of this study, drug-eluting stents were not available in the same size ranges as non-drug-eluting stents. Small-vessel stenting is associated with higher risks during follow-up and during the procedure. Therefore, because the study was not randomized, treatment choices may have been influenced by stent availability.

### Superficial Venous Thrombosis: Prevalence of Common Genetic Risk Factors and Their Role on Spreading to Deep Veins

Milio G, Siragusa S, Mina C, et al. *Thromb Res* 2008;123:194-9.

**Conclusion:** There is a high presence of genetic mutations (factor V Leiden, prothrombin G20210A mutation, and 5,10-methylenetetrahydrofolate reductase [MTHFR C677T]) in patients with superficial venous thrombosis (SVT) occurring in normal veins.

**Summary:** SVT that occurs in varicose veins is considered of low clinical relevance because of the generally favorable outcome. SVT occurring in so-called healthy veins represents only approximately 25% of all SVT. This type of SVT is generally considered of greater clinical relevance because it has been associated with various neoplastic conditions. It is also known that SVT occurring in so-called healthy veins can progress into the deep system. Depending on the study, propagation into deep veins is about 3% to 15%. Genetic abnormalities of coagulation can also predispose to SVT. Less well studied is whether the presence of a genetic coagulation abnormality occurring in patients with SVT predisposes them to progression into the deep system.

In this study the authors evaluated 107 patients with SVT and no other obvious risk factors. They used ultrasound examinations to document progression into the deep system and tested for the presence of factor V Leiden, prothrombin G20210A mutation, and MTHFR C677T mutations. In the patients with SVT in normal veins, factor V Leiden was present in 26.3% when the thrombus was limited to the superficial veins and was present in 60% of SVT that extended into the deep system. Prothrombin gene mutation was found in 7.9% of SVT limited to the superficial system and in 20% where SVT progressed to the deep system. MTHFR C677T mutation was found in 23.7% of patients with SVT limited to the superficial system and in 40% where SVT progressed to the deep system. In patients with SVT occurring in varicose veins, the presence of these abnormalities was less common (6.7%, 4.4%, and 6.7% respectively). If, however, the SVT from the varicose veins spread to the deep system, prevalence of genetic abnormalities was considerably higher (13.5% factor V Leiden mutation, 7.4% prothrombin gene mutation, and 21.4% MTHFR C677T mutation).

**Comment:** This article paper provides guidance on which patients with SVT should undergo a thrombophilia evaluation. Whereas patients with SVT occurring in normal veins were previously recognized as having a reasonably high incidence of genetic coagulation abnormalities, this report points out that those patients who have SVT in varicose veins that extends into the deep system have a significant prevalence of genetic abnormalities as well. SVT patients appropriate for thrombophilia workup are those where the SVT occurs in normal veins and those with SVT in varicose veins that extends into the deep system.

### Low-Dose Aspirin for Primary Prevention of Atherosclerotic Events in Patients with Type 2 Diabetes: A Randomized Controlled Trial

Ogawa H, Nakayama M, Morimoto T, et al. *JAMA* 2008;301:2134-41.

**Conclusion:** Low-dose aspirin as primary prevention does not reduce the risk of cardiovascular events in patients with type 2 diabetes.

**Summary:** In patients with previous cardiovascular events, aspirin therapy can serve as a secondary prevention strategy. Clinical guidelines also recommend patients with risk factors for coronary heart disease should take aspirin for primary prevention. However, subgroup analyses of large trials of aspirin for primary prevention have not demonstrated significant effects in patients with diabetes. Because these analyses were subgroup analyses, it is possible they were underpowered to demonstrate primary prevention of cardiovascular events with aspirin in patients with diabetes.

The Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD) Trial is reported here. The objective was to determine